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# Cloning of the endothelial cell tropic and leukotropic clinical isolate VR1814 as FIX-BAC

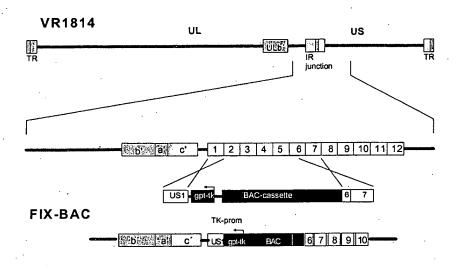


Fig. 1 Construction of FIX-BAC. A gpt-tk-BAC cassette was introduced into the US2-6 region of the parental virus VR1814 as described in patent application PCT/EP02/01867 (WO 02/066629).

Figure 2

RVFIX virus mutants RVFIXΔULb' RVFIXΔUL132-128 RVFIXΔUL133-148	<b>Deletion</b> according to (Cheent 175662-189347 nt 174857-176865 nt 177896-189347	e, Bankier et al., 1990)
RVFIXAUL132-130 RVFIXAUL131K RVFIXAUL130 RVFIXAUL128K RVFIXAUL132K	nt 177696-169347 nt 175662-177743 nt 176377-176776 nt 175662-176314 nt 174953-175387 nt 177076-177752 nt 177896-178644 nt 179069-179966 nt 174467-174770	Fig. 2 List of RVFI mutants and determine the mutation (kar cassette insertion) act to annotation by Bankier, et al. 1990 26

Fig. 2 List of RVFIX virus mutants and determination of mutation (kanamycin cassette insertion) according to annotation by {Chee, Bankier, et al. 1990 269 /id} Figure 3 shows an agarse gel and Southern Blot of RVFIX and RVFIX mutant viruses.

Figure 3

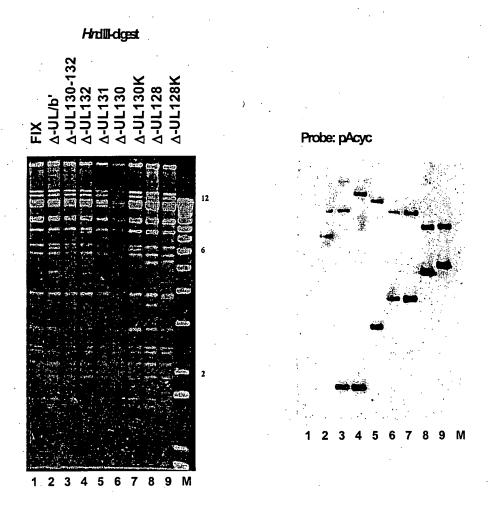


Fig.3 DNA derived from individually grown FIX-BAC clones (lane 1) or FIX-BAC mutant clones  $\Delta ULb'$ ,  $\Delta UL130$ -132,  $\Delta UL132$ ,  $\Delta UL131$ ,  $\Delta UL130$ ,  $\Delta UL130$ K,  $\Delta UL128$  and  $\Delta UL128$ K (lanes 2-9) was digested with *Hind*III and run on a 0.5% agarose gel.

A	
FIX 176834 RACE_95_3 RACE_95_8 RACE_95_11	-GTCTGCAACATGCGGCTGTGTCGGGTGTGGCTGTTTTTTTT
FIX RACE_95_3 RACE_95_8 RACE_95_11	GGTCAGTGCCAGCGGGAGACCGCAGAAAAAAACGATTATTACCGAGTACCGCATTACT GGTCAGTGCCAGCGGGAGACCGCAGAAAAAAACGATTATTACCGAGTACCGCATTACT GGTCAGTGCCAGCGGGAGACCGCAGAAAAAAACGATTATTACCGAGTACCGCATTACT GGTCAGTGCCAGCGGGAGACCGCAGAAAAAAAA-CGATTATTACCGAGTACCGCATTACT
FIX RACE_95_3 RACE_95_8 RACE_95_11	GGGACGCGTGCTCTCGCGCGCTGCCTGACCAAACCCGTTACAAGTATGTGGAACAGCTCG GGGACGCGTGCTCTCGCGCGCTGCCTGACCAAACCCGTTACAAGTATGTGGAACAGCTCG GGGACGCGTGCTCTCGCGCGCTGCCTGACCAAACCCGTTACAAGTATGTGGAACAGCTCG GGGACGCGTGCTCTCGCGCGCTGCCTGACCAAACCCGTTACAAGTATGTGGAACAGCTCG
FIX RACE_95_3 RACE_95_8 RACE_95_11	TGGACCTCACGTTGAACTACCACTACGATGCGAGCCACGGCTTGGACAACTTTGACGTGC TGGACCTCACGTTGAACTACCACTACGATGCGAGCCACGGCTTGGACAACTTTGACGTGC TGGACCTCACGTTGAACTACCACTACGATGCGAGCCACGGCTTGGACAACTTTGACGTGC TGGACCTCACGTTGAACTACCACTACGATGCGAGCCACGGCTTGGACAACTTTGACGTGC
FIX RACE_95_3 RACE_95_8 RACE_95_11	TCAAGAGTGAGGGTACGCGCTAAAGGTGTATGACAACGGGAAGGTAAGGGCGAACGGGT TCAAGAGTTGAGGGTACGCGCTAAAGGTGTATGACAACGGGAAGGTAAGGGCGAACGGGT TCAAGAGTTATGACAACGGGAAGGTAAGGGCGAACGGGT TCAAGAG
FIX RACE_95_3 RACE_95_8 RACE_95_11	AACGGGTAGCTAACCGCATGGGGTGTGAAATGACGTTCGGAACCTGTGCTTGCÄGAATCAAATCA AACGGGTAGCTAACCGCATGGGGTGTGAAATGACGTTCGGAACCTGTGCTTGCÄGAATCAAATCA
FIX RACE_95_3 RACE_95_8 RACE_95_11	ACGTGACCGAGGTGTCGTTGCTCATCAGCGACTTTAGACGTCAGAACCGTCGCGGCGGCA ACGTGACCGAGGTGTCGTTGCTCATCAGCGACTTTATACGTCAGAACCGTCGCGGCGGCA ACGTGACCGAGGTGTCGTTGCTCATCAGCGACTTTAGACGTCAGAACCGTCGCGGCGCA ACGTGACCGAGGTGTCGTTGCTCATCAGCGACTTTAGACGTCAGAACCGTCGCGGCGGCA
FIX RACE_95_3 RACE_95_8 RACE_95_11	CCAACAAAAGGACCACGTTCAACGCCGCCGGTTCGCTGGCGCCTCACGCCCGGAGCCTCG CCAACAAAAGGACCACGTTCAACGCCGCCGGTTCGCTGGCGCCTCACGCCCGGAGCCTCG CCAACAAAAGGACCACGTTCAACGCCGCCGGTTCGCTGGCGCCTCACGCCCGGAGCCTCG CCAACAAAAGGACCACGTTCAACGCCGCCGGTTCGCTGGCGCCTCACGCCCGGAGCCTCG
FIX RACE_95_3 RACE_95_8 RACE_95_11	AGTTCAGCGTGCGGCTCTTTGCCAACTAGCCTGCGTCA-176346 AGTTCAGCGTGCGGCTCTTTGCCAACTAGCCTGCGTCA AGTTCAGCGTGCGGCTCTTTGCCAACTAGCCTGCGTCA AGTTCAGCGTGCGGCTCTTTGCCAACTAGCCTGCGTCA
В	
FIX 175631- RACE_95_3 RACE_95_8 RACE_95_13	-CCGCGCGTCATGAGTCCCAAAAACCTGACGCCGTTCTTGACGGCGTTGTGGCTGCTATTG CCGTGCGTCATGAGTCCCAAAAACCTGACGCCGTTCTTGACGGCGTTGTGGCTGCTATTG CCGCGCGTCATGAGTCCCAAAAACCTGACGCCGTTCTTGACGGCGTTGTGGCTGCTATTG CCGCGCGTCATGAGTCCCAAAAACCTGACGCCGTTCTTGACGGCGTTGTGGCTGCTATTG
FIX7 RACE_95_3 RACE_95_8 RACE_95_11	GGTCACAGCCGCGTGCCGCGGGTACGCGCAGAAGAATGTTGCGAATTCATAAACGTCAAC GGTCACAGCCGCGTGCCGCGGTACGCGCAGAAGAATGTTGGGAATTCATAAACGTCAAC GGTCACAGCCGCGTGCCGCGGTACGCGCAGAAGAATGTTGCGAATTCATAAACGTCAAC GGTCACAGCCGCGCGCGCGCAGCAAGAAGAATGTTGCGAATTCATAAACGTCAAC

FIX RACE_95_3 RACE_95_8 RACE_95_11	CACCCGCCGGAACGCTGTTACGATTTCAAAATGTGCAATCGCTTCACCGTCGCGTACGTA
FIX RACE_95_3 RACE_95_8 RACE_95_11	TTTTTATGATTGTCTGCGTTCTGTGGTGCGTCTGGATTTGTCTCTCGACGTTTCTGATAG TTTTCATGATTGTCTGCGTTCTGTGGTGCGTCTGGATCTGTCTCTCGACGTTTCTGATAG TTTTCATGATTGTCTGCGTTCTGTGGTGCGTCTGGATCTGTCTCTCTGACGTTTCTGATAG
FIX RACE_95_3 RACE_95_8 RACE_95_11	CCATGTTCCATCGACGATCCTCGGGAATGCCAGAGTAGATTTTCATGAATCCACAGGCTG CCATGTTCCATCGACGATCCTCGGGAATGCCAGAGTAGATTTTCATGAATCCACAGGCTG CCATGTTCCATCGACGATCCTCGGGAATGCCAGAGTAGATTTTCATGAATCCACAGGCTG
FIX RACE_95_3 RACE_95_8 RACE_95_11	CGGTGTCCGGACGCGAAGTCTGCTACAGTCCCGAGAAAACGGCTGAGATTCGCGGGATC CGGTGTCCGGACGCGAAGTCTGCTACAGTCCCGAGAAAACGGCTGAGATTCGCGGGATC CGGTGTCCGGACGGCGAAGTCTGCTACAGTCCCGAGAAAACGGCTGAGATTCGCGGGATC CGGTGTCCGGACGGCGAAGTCTGCTACAGTCCCGAGAAAACGGCTGAGATTCGCGGGATC
FIX RACE_95_3 RACE_95_8 RACE_95_11	GTCACCACCATGACCCATTCATTGACACGCCAGGTCGTACACAACAACTGACGAGCTGC GTCACCACCATGACCCATTCATTGACACGCCAGGTCGTACACAAACAA
FIX RACE_95_3 RACE_95_8 RACE_95_11	AACTACAATCCGTAAGTCTCTTCCTCGAGGGCCTTACAGCCTATGGGAAAGTAAGACAGA AACTACAATCCAACTACAATCCAACTACAATCCAACTACAATCC
FIX RACE_95_3 RACE_95_8 RACE_95_11	GGGACAAAACATCATTAAAAAAAAAGTCTAATTTCACGTTTTGTACCCCCCCTTCCCCTC
FIX RACE_95_3 RACE_95_8 RACE_95_11	CGTGTTGTAGGTTATACCTCGAAGCTGACGGGCGAATACGCTGCGGCAAAGTGAACGACAGTTATACCTCGAAGCTGACGGCGAATACGCTGCGGCAAAGTGAACGACAGTTATACCTCGAAGCTGACGGCGAATACGCTGCGGCAAAGTGAACGACAGTTATACCTCGAAGCTGACGGGCGAATACGCTGCGGCAAAGTGAACGACA
FIX RACE_95_3 RACE_95_8 RACE_95_11	AGGCGCAGTACCTGCTGGGCGCCGCTGGCAGCGTTCCCTATCGATGGATCAACCTGGAAT AGGCGCAGTACCTGCTGGGCGCCGCTGGCAGCGTTCCCTATCGATGGATCAACCTGGAAT AGGCGCAGTACCTGCTGGGCGCCGCTGGCGCGTTCCCTATCGATGGATCAACCTGGAAT AGGCGCAGTACCTGCTGGGCGCCGCTGGCAGCGTTCCCTATCGATGGATCAACCTGGAAT
FIX RACE_95_3 RACE_95_8 RACE_95_11	ACGACAAGATAACCCGGATCGTGGGCCTGGATCAGTACCTGGAGAGCGTTAAGAAACACA ACGACAAGATAACCCGGATCGTGGGCCTGGATCAGTACCTGGAGAGCGTTAAGAAACACA ACGACAAGATAGCCCGGATCGTGGGCCTGGATCAGTACCTGGAGAGCGTTAAGAAACACA ACGACAAGATAACCCGGATCGTGGGCCTGGATCAGTACCTGGAGAGCGTTAAGAAATACA
FIX RACE_95_3 RACE_95_8 RACE_95_11	AACGGCTGGATGTGCCCGCGCTAAAATGGGCTATATGCTGCAG <b>TGA</b> ATAATAAA-174887 AACGGCTGGATGTGCCGCGCTAAAATGGGCTATATGCTGCAG <b>TGA</b> ATAATAAA AACGGCTGGATGTGCCGCGCTAAAATGGGCTATATGCTGCAG <b>TGA</b> ATAATAAA AACGGCTGGATGTGCCGCGCTAAAATGGGCTATATGCTGCAG <b>TGA</b> ATAATAAA

FIX

RACE_95_3	CGCTAAAATGGGCTATATGCTGCAG <b>TGA</b> AT <u>AATAAA</u> ATGTGTGTTTTGTCC <b>G</b> CAAAAAAAA
RACE_95_8	CGCTAAAATGGGCTATATGCTGCAGT AATAATAAAAATGTGTGTTTTGTCCAAAAAAAAAA
RACE_95_11	CGCTAAAATGGGCTATATGCTGCAGTGAATAAAAATGTGTGTG

Fig. 4 UL131-128 mRNA processing — Panels (A-C) compare FIX-BAC DNA sequence (numbered according to Chee et al.) to a set of cDNA sequences from RACE clones 95-3, 95-8 and 95-11 (A) UL131 region, (B) UL128 region, (C) UL131-128 transcripts 3' end. Start codons, stop codons and the polyA site are in bold face, mRNA processing signals (splice donor sequence, splice acceptor sequence, AATAAA signal) are grey-shaded.

Figure 5

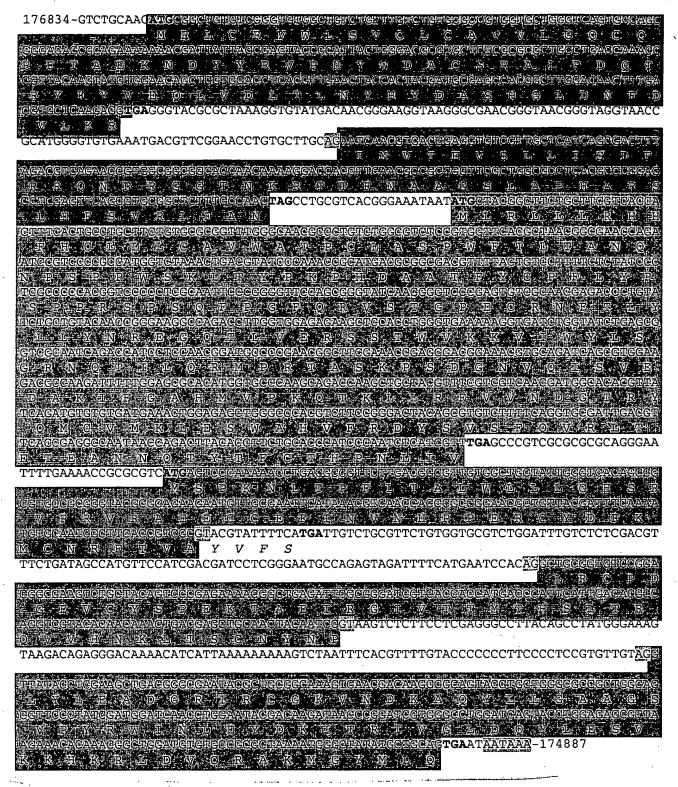


Fig. 5 Exon-intron organization of the FIX-BAC UL131-128 genetic locus. UL131 (green); UL130 (orange); UL128 (blue); UL128x1 C-terminus (light blue).

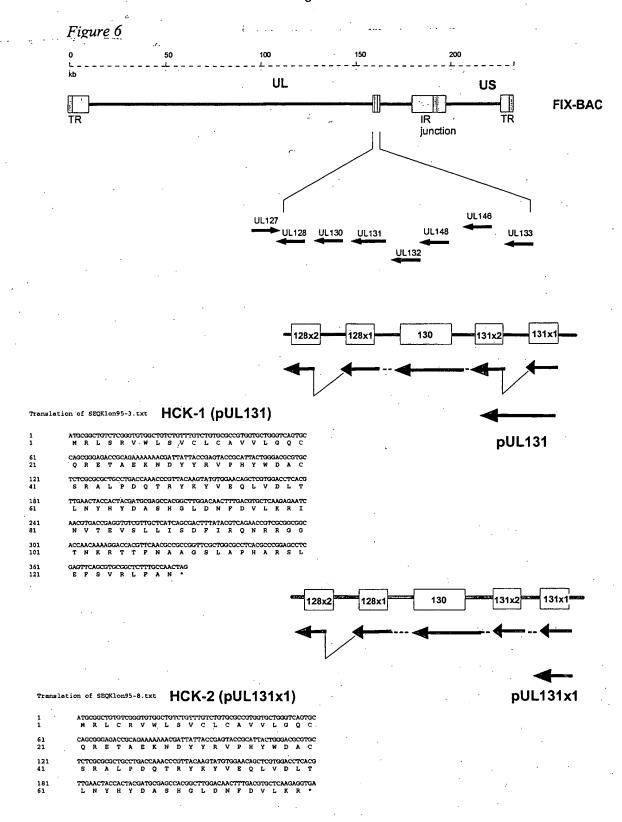
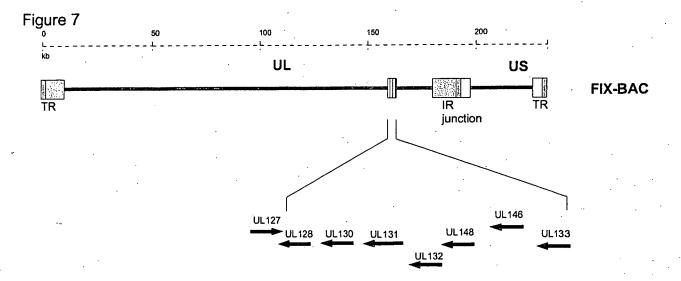
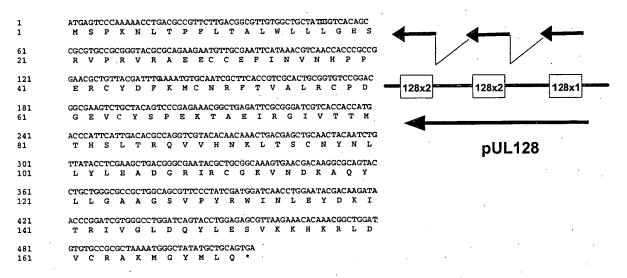


Fig. 6 Scheme of the differentially spliced transcripts of the UL131-128 region. Upper panel RACE clone 95-3 and predicted open reading frame (orf) pUL131 (HCK-1). Lower panel RACE clone 95-8 and predicted orf UL131x1 (HCK-2).



#### Translation of SEQ128.txt(1-563: HCK-4 (pUL128)



#### Translation of SEQ128 x 1txt HCK-3 (pUL128x1)

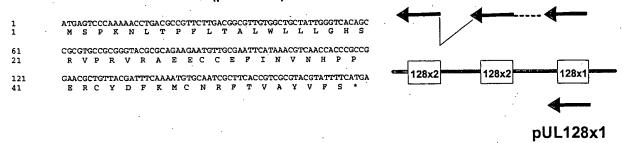


Fig. 7 Scheme of the differentially spliced transcripts of the UL131-128 region. Upper panel SEQUL128B and predicted open reading frame (orf) pUL128 (HCK-4). Lower panel SEQUL128A and predicted orf UL128x1 (HCK-3).

## **Northern Blot Analyses**

### **RVFIX**, **RVFIX** mutants and laboratory strains:

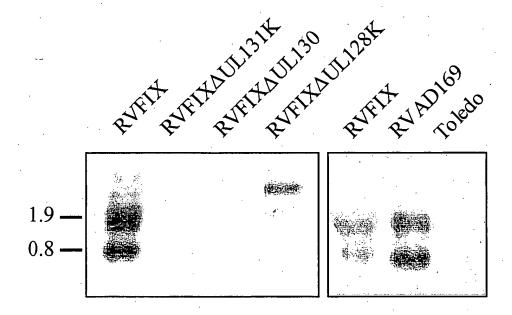


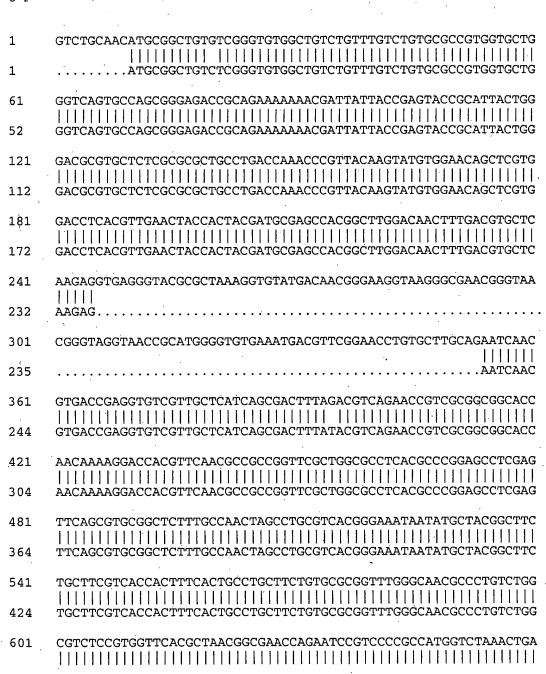
Fig. 8 mRNA was prepared from RVFIX-infected fibroblasts 4 days p.i. using Rneasy Mini, QIAshredder and Oligotex mRNA Mini kits according to the manufacturer's guidance (Qiagen). For Nothern blotting, 1  $\mu$ g RNA was electrophoresed on an agarose gel according to the MOPS-formaldehyde protocol and blotted onto Hybond N+ membranes (Amersham Pharmacia). Blots were hybridized with a UL131-128 specific probe.

Figure 9

#### Comparison RACE clone 95-3 – FIX genomic sequence

Upper line: SEQFIX UL131-128.txt, from 10 to 1977 Lower line: SEQKlon95-3.txt, from 1 to 1741

SEQFIX UL131-128.txt:SEQKlon95-3.txt identity= 99.66%(1735/1741) gap=11.94%(236/1977)



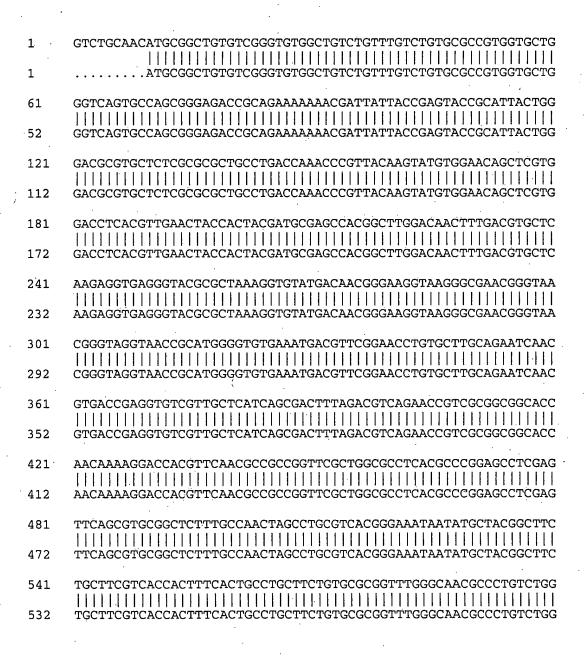
484	CGTCTCCGTGGTTCACGCTAACGGCGAACCAGAATCCGTCCCCGCCATGGTCTAAACTGA
661 544	CGTATCCCAAACCGCATGACGCGGCGACGTTTTACTGTCCTTTTCTCTATCCCTCGCCCC
721	CACGGTCCCCTCGCAATTCCCGGGGTTCCAGCGGGTATCAACGGGTCCCGAGTGTCGCA
604	CACGGTCCCCTCGCAATTCCCGGGGTTCCAGCGGTATCAACGGGTCCCGAGTGTCGCA
781 664	ACGAGACCCTGTATCTGCTGTACAACCGGGAAGGCCAGACCTTGGTGGAGAGAAGCTCCA
841	CCTGGGTGAAAAAGGTGATCTGGTATCTGAGCGGTCGCAATCAGACCATCCTCCAACGGA
724	
901	TGCCCGAACGGCTTCGAAACCGAGCGACGGAAACGTGCAGATCAGCGTGGAAGACGCCA
784	TGCCCCGAACGGCTTCGAAACCGAGCGACGGAAACGTGCAGATCAGCGTGGAAGACGCCA
961	AGATTTTTGGAGCGCACATGGTGCCCAAGCAGACCAAGCTGCTACGTTTCGTCGTCAACG
844	AGATTTTTGGAGCGCACATGGTGCCCAAGCAGACCAAGCTGCTACGTTTCGTCGCCAACG
904	ATGGCACACGTTATCAGATGTGTGTGATGAAACTGGAGAGCTGGGCCCACGTCTTCCGGG
1081	ACTACAGCGTGTCTTTTCAGGTGCGATTGACGTTCACCGAGGCCAATAACCAGACTTACA
964	
1141	CCTTCTGCACCCATCCCAATCTCATCGTTTGAGCCCGTCGCGCGCG
1024	CCTTCTGCACCCATCCCAATCTCATCGTTTGAGCCCGTCGCGCGCG
1201	AACCGCGCGTCATGAGTCCCAAAAACCTGACGCCGTTCTTGACGGCGTTGTGGCTGCTAT
1084	AACCGTGCGTCATGAGTCCCAAAAACCTGACGCCGTTCTTGACGGCGTTGTGGCTGCTAT
1261	TGGGTCACAGCCGCGTGCCGCGGGTACGCGCAGAAGAATGTTGCGAATTCATAAACGTCA
1144	TGGGTCACAGCCGCGTGCCGCGGGTACGCGCAGAAGAATGTTGCGAATTCATAAACGTCA
1321	ACCACCGGCGGAACGCTGTTACGATTTCAAAATGTGCAATCGCTTCACCGTCGCGTACG
1204	ACCACCGGCGGAACGCTGTTACGATTTCAAAATGTGCAATCGCTTCACCGTCGCGTACG
1381	TATTTTCATGATTGTCTGCGTTCTGTGGTGCGTCTGGATTTGTCTCTCGACGTTTCTGAT
1264	TATTTTCATGATTGTCTGCGTTCTGTGGTGCGTCTGGATCTGTCTCTCGACGTTTCTGAT
1441	AGCCATGTTCCATCGACGATCCTCGGGAATGCCAGAGTAGATTTTCATGAATCCACAGGC
1324	AGCCATGTTCCATCGACGATCCTCGGGAATGCCAGAGTAGATTTTCATGAATCCACAGGC

1501	TGCGGTGTCCGGACGGCGAAGTCTGCTACAGTCCCGAGAAAACGGCTGAGATTCGCGGGA
1384	TGCGGTGTCCGGACGCGAAGTCTGCTACAGTCCCGAGAAAACGGCTGAGATTCGCGGGA
1561	TCGTCACCACCATGACCCATTCATTGACACGCCAGGTCGTACACAACAAACTGACGAGCT
1444	TCGTCACCACCATGACCCATTCATTGACACGCCAGGTCGTACACAACAAACTGACGAACT
1621	GCAACTACAATCCGTAAGTCTCTTCCTCGAGGGCCTTACAGCCTATGGGAAAGTAAGACA
1504	GCAACTACAATCC
1681	GAGGGACAAAACATCATTAAAAAAAAAGTCTAATTTCACGTTTTGTACCCCCCCTTCCCC
1517	
1741	TCCGTGTTGTAGGTTATACCTCGAAGCTGACGGCGAATACGCTGCGGCAAAGTGAACGA
1517	
1801	CAAGGCGCAGTACCTGCTGGGCGCCGCTGGCAGCGTTCCCTATCGATGGATCAACCTGGA
1565	CAAGGCGCAGTACCTGCTGGGCGCCCCTGGCAGCGTTCCCTATCGATGGATCAACCTGGA
1861	ATACGACAAGATAACCCGGATCGTGGGCCTGGATCAGTACCTGGAGAGCGTTAAGAAACA
1625	ATACGACAAGATAACCCGGATCGTGGGCCTGGATCAGTACCTGGAGAGCGTTAAGAAACA
1921	CAAACGGCTGGATGTGCCGCGCTAAAATGGGCTATATGCTGCAGTGAATAATAAA
1685	
Trans	CAAACGGCTGGATGTGCCGCGCTAAAATGGGCTATATGCTGCAGTGAATAATAAA  slation of SEQKlon95-3.txt: HCK-1 (pUL131)  ATGCGGCTGTCTCGGGTGTGGCTGTTTTGTCTGTGCGCCGTGGTG
Trans	CAAACGGCTGGATGTGCCGCGCTAAAATGGGCTATATGCTGCAGTGAATAATAAA  Slation of SEQKlon95-3.txt: HCK-1 (pUL131)  ATGCGGCTGTCTCGGGTGTGGCTGTCTGTTTGTCTGTGCGCCGTGGTG
Trans	CAAACGGCTGGATGTGCCGCGCTAAAATGGGCTATATGCTGCAGTGAATAATAAA  slation of SEQKlon95-3.txt: HCK-1 (pUL131)  ATGCGGCTGTCTCGGGTGTGGCTGTTTTGTCTGTGCGCCGTGGTG
Trans  1  1  61  21  121	CAAACGGCTGGATGTGTGCCGCGCTAAAATGGGCTATATGCTGCAGTGAATAATAAA  Slation of SEQKlon95-3.txt: HCK-1 (pUL131)  ATGCGGCTGTCTCGGGTGTGGCTGTCTGTTTGTCTGTGCGCCGTGGTG
Trans  1  1  61  21  121  41	CAAACGGCTGGATGTGTGCCGCGCTAAAATGGGCTATATGCTGCAGTGAATAATAAA  Slation of SEQKlon95-3.txt: HCK-1 (pUL131)  ATGCGGCTGTCTCGGGTGTGGCTGTCTGTTTGTCTGTGCGCCGTGGTG
Trans  1  1  61  21  121	CAAACGGCTGGATGTGTGCCGCGCTAAAATGGGCTATATGCTGCAGTGAATAATAAA  Slation of SEQKlon95-3.txt: HCK-1 (pUL131)  ATGCGGCTGTCTCGGGTGTGGCTGTCTGTTTGTCTGTGCGCCGTGGTG
Trans  1  1  61 21  121 41  181 61  241	CAAACGCTGGATGTGTGCCGCGCTAAAATGGGCTATATGCTGCAGTGAATAATAAA  Slation of SEQKlon95-3.txt: HCK-1 (pUL131)  ATGCGGCTGTCTCGGGTGTGGCTGTTTGTCTGTGCGCCGTGGTG
Trans  1  1  61  21  121  41  181  61	CAAACGCTGGATGTGCCGCGCTAAAATGGGCTATATGCTGCAGTGAATAATAAA  Slation of SEQKlon95-3.txt: HCK-1 (pUL131)  ATGCGGCTGTCTCGGGTGTGGCTGTCTGTTTGTCTGTGCGCCGTGGTG
Trans  1  1  61 21  121 41  181 61  241 81	CAAACGCTGGATGTGCCGCGCTAAAATGGGCTATATGCTGCAGTGAATAATAAA  Slation of SEQKlon95-3.txt: HCK-1 (pUL131)  ATGCGGCTGTCTCGGGTGTGGCTGTCTGTTTGTCTGTGCGCCGTGGTG
Trans  1  1  61 21  121 41  181 61  241 81	CAAACGCTGGATGTGTGCCGCGCTAAAATGGGCTATATGCTGCAGTGAATAATAAA  Slation of SEQKlon95-3.txt: HCK-1 (pUL131)  ATGCGGCTGTCTCGGGTGTGGCTGTCTGTTTGTCTGTGCGCCGTGGTG

#### Comparison RACE clone 95-8 -FIX genomic sequence

Upper line: SEQFIX UL131-128.txt, from 10 to 1977 Lower line: SEQKlon95-8.txt, from 1 to 1849

SEQFIX UL131-128.txt:SEQKlon95-8.txt identity= 99.78%(1845/1849) gap=6.47%(128/1977)



601 592	CGTCTCCGTGGTTCACGCTAACGGCGAACCAGAATCCGTCCCCGCCATGGTCTAAACTGA
661	CGTATCCCAAACCGCATGACGCGGCGACGTTTTACTGTCCTTTTCTCTATCCCTCGCCCC
652	CGTATCCCAAACCGCATGACGCGGCGACGTTTTACTGTCCTTTTCTCTATCCCTCGCCCC
721 712	CACGGTCCCCTCGCAATTCCCGGGGTTCCAGCGGGTATCAACGGGTCCCGAGTGTCGCA
781	ACGAGACCCTGTATCTGCTGTACAACCGGGAAGGCCAGACCTTGGTGGAGAGAAGCTCCA
772	
341	CCTGGGTGAAAAAGGTGATCTGGTATCTGAGCGGTCGCAATCAGACCATCCTCCAACGGA
332	CCTGGGTGAAAAAGGTGATCTGGTATCTGAGCGGTCGCAATCAGACCATCCTCCAACGGA
901	TGCCCCGAACGGCTTCGAAACCGAGCGACGGAAACGTGCAGATCAGCGTGGAAGACGCCA
392	TGCCCCGAACGGCTTCGAAACCGAGCGACGGAAACGTGCAGATCAGCGTGGAAGACGCCA
961 952	AGATTTTTGGAGCGCACATGGTGCCCAAGCAGACCAAGCTGCTACGTTTCGTCGTCAACG
1021	ATGGCACACGTTATCAGATGTGTGTGATGAAACTGGAGAGCTGGGCCCACGTCTTCCGGG
1012	
1081	ACTACAGCGTGTCTTTTCAGGTGCGATTGACGTTCACCGAGGCCAATAACCAGACTTACA
1072	ACTACAGCGTGTCTTTTCAGGTGCGATTGACGTTCACCGAGGCCGATAACCAGACTTACA
1141	CCTTCTGCACCCATCCCAATCTCATCGTTTGAGCCCGTCGCGCGCG
1132	CCTTCTGCACCCATCCCAATCTCATCGTTTGAGCCCGTCGCGCGCG
1201	AACCGCGCGTCATGAGTCCCAAAAACCTGACGCCGTTCTTGACGGCGTTGTGGCTGTAT
1192	AACCGCGCGTCATGAGTCCCAAAAACCTGACGCCGTTCTTGACGGCGTTGTGGCTGCTAT
1261 1252	TGGGTCACAGCCGCGTGCCGCGGGTACGCGCAGAAGAATGTTGCGAATTCATAAACGTCA
1321	ACCACCGCGGAACGCTGTTACGATTTCAAAATGTGCAATCGCTTCACCGTCGCGTACG
1312	ACCACCGGCGGAACGCTGTTACGATTTCAAAATGTGCAATCGCTTCACCGTCGCGTACG
1381	TATTTTCATGATTGTCTGCGTTCTGTGGTGCGTCTGGATTTGTCTCTCGACGTTTCTGAT
1372	TATTTTCATGATTGTCTGCGTTCTGTGGTGCGTCTGGATCTGTCTCTCGACGTTTCTGAT

1441 1432	AGCCATGTTCCATCGACGATCCTCGGGAATGCCAGAGTAGATTTTCATGAATCCACAGGC
1501	TGCGGTGTCCGGACGCGAAGTCTGCTACAGTCCCGAGAAAACGGCTGAGATTCGCGGGA
1492	TGCGGTGTCCGGACGCGAAGTCTGCTACAGTCCCGAGAAAACGGCTGAGATTCGCGGGA
1561	TCGTCACCACCATGACCCATTCATTGACACGCCAGGTCGTACACAACAAACTGACGAGCT
1552	TCGTCACCACCATGACCCATTCATTGACACGCCAGGTCGTACACAAAACTGACGAGCT
1621	GCAACTACAATCCGTAAGTCTCTTCCTCGAGGGCCTTACAGCCTATGGGAAAGTAAGACA
1612	GCAACTACAATCC
1681	GAGGGACAAAACATCATTAAAAAAAAAGTCTAATTTCACGTTTTGTACCCCCCCTTCCCC
1625	
1741	TCCGTGTTGTAGGTTATACCTCGAAGCTGACGGGCGAATACGCTGCGGCAAAGTGAACGA
1625	GTTATACCTCGAAGCTGACGGGCGAATACGCTGCGGCAAAGTGAACGA
1801	CAAGGCGCAGTACCTGCTGGGCGCCGCTGGCAGCGTTCCCTATCGATGGATCAACCTGGA
1673	CAAGGCGCAGTACCTGCTGGGCGCCCTGGCGGCGTTCCCTATCGATGGATCAACCTGGA
1861	ATACGACAAGATAACCCGGATCGTGGGCCTGGATCAGTACCTGGAGAGCGTTAAGAAACA
1733	ATACGACAAGATAGCCCGGATCGTGGGCCTGGATCAGTACCTGGAGAGCGTTAAGAAACA
1921	CAAACGGCTGGATGTGTGCCGCGCTAAAATGGGCTATATGCTGCAGTGAATÁATAAA
1793	CAAACGGCTGGATGTGCCGCGCTAAAATGGGCTATATGCTGCAGTGAATAATAAA

# Translation of SEQKlon95-8.txt: HCK-2 (pUL131x1)

1	ATGCGGCTGTGTCGGGTGTGCTGTTTGTCTGTGCGCCGTGGTG
1	MRLCRVWLSVCLCAVVLGQC
61	CAGCGGGAGACCGCAGAAAAAACGATTATTACCGAGTACCGCATTACTGGGACGCGTGC
21	Q R E T A E K 🗓 D Y Y R V P H Y W D A C
121	TCTCGCGCGCTGCCTGACCAAACCCGTTACAAGTATGTGGAACAGCTCGTGGACCTCACG
41	S R A L P D Q T R Y K Y V E Q L V D L T
181	TTGAACTACCACTACGATGCGAGCCACGGCTTGGACAACTTTGACGTGCTCAAGAGGTGA
61	L N Y H Y D A S H G L D N F D V L K R *

## Comparison RACE clone 95-11 -FIX genomic sequence

Upper line: SEQFIX UL131-128.txt, from 10 to 1977 Lower line: SEQKlon95-11.txt, from 1 to 1620

SEQFIX UL131-128.txt:SEQKlon95-11.txt identity= 99.57%(1611/1618) gap=18.24%(361/1979)

1	GTCTGCAACATGCGGCTGTCTCGGGTGTGCTCTGTTTGTCTGTGCGCCGTGGTG
1	ATGCGGCTGTCTGGGTGTGGCTGTCTGTTTGTCTGTGCGCCGTGGTG
61	GGTCAGTGCCAGCGGGAGACCGCAGAAAAAAACGATTATTACCGAGTACCGCATTACT
52	GGTCAGTGCCAGCGGGAGACCGCAGAAAAAAAACGATTATTACCGAGTACCGCATTACT
119	GGGACGCGTGCTCTCGCGCGCTGCCTGACCAAACCCGTTACAAGTATGTGGAACAGCTCG
112	GGGACGCGTGCTCGCGCGCTGCCTGACCAAACCCGTTACAAGTATGTGGAACAGCTCG
179	TGGACCTCACGTTGAACTACCACTACGATGCGAGCCACGGCTTGGACAACTTTGACGTGC
172	TGGACCTCACGTTGAACTACCACTACGATGCGAGCCACGGCTTGGACAACTTTGACGTGC
239	TCAAGAGGTGAGGGTACGCGCTAAAGGTGTATGACAACGGGAAGGTAAGGGCGAACGGGT
232	TCAAGAG
299	AACGGGTAGGTAACCGCATGGGGTGTGAAATGACGTTCGGAACCTGTGCTTGCAGAATCA
237	AATCA
359	ACGTGACCGAGGTGTCGTTGCTCATCAGCGACTTTAGACGTCAGAACCGTCGCGGCGCA
244	ACGTGACCGAGGTGTCGTTGCTCATCAGCGACTTTAGACGTCAGAACCGTCGCGGCGGCA
419	CCAACAAAAGGACCACGTTCAACGCCGCCGGTTCGCTGGCGCCTCACGCCCGGAGCCTCG
304	CCAACAAAAGGACCACGTTCAACGCCGCCGGTTCGCTGGCGCCTCACGCCCGGAGCCTCG
479	AGTTCAGCGTGCGGCTCTTTGCCAACTAGCCTGCGTCACGGGAAATAATATGCTACGGCT
364	AGTTCAGCGTGCGGCTCTTTGCCAACTAGCCTGCGTCACGGGAAATAATATGCTACGGCT
539	${\tt TCTGCTTCGTCACCACTTTCACTGCCTGCTTCTGTGCGCGGTTTGGGCAACGCCCTGTCT}$

424	TCTGCTTCGTCACCACTTTCACTGCCTGCTTCTGTGCGCGGTTTGGGCAACGCCCTGTCT
599	GGCGTCTCCGTGGTTCACGCTAACGGCGAACCAGAATCCGTCCCCGCCATGGTCTAAACT
484 659	GGCGTCTCCGTGGTTCACGCTAACGGCGAACCAGAATCCGTCCCCGCCATGGTCTAAACT GACGTATCCCAAACCGCATGACGCGGCGACGTTTTACTGTCCTTTTCTCTATCCCTCGCC
544	GACGTATCCCAAACCGCATGACGCGGCGACGTTTTACTGTCCTTTTCTCTATCCCTCGCC
719 604	CCCACGGTCCCCTCGCAATTCCCGGGGTTCCAGCGGGTATCAACGGGTCCCGAGTGTCG
779 664	CAACGAGACCCTGTATCTGCTGTACAACCGGGAAGGCCAGAĆCTTGGTGGAGAGAAGCTC
839	CACCTGGGTGAAAAAGGTGATCTGGTATCTGAGCGGTCGCAATCAGACCATCCTCCAACG
724	
399 784	GATGCCCCGAACGGCTTCGAAACCGAGCGACGGAAACGTGCAGATCAGCGTGGAAGACGC
959 344	CAAGATTTTTGGAGCGCACATGGTGCCCAAGCAGACCAAGCTGCTACGTTTCGTCGTCAA
1019 904	CGATGGCACACGTTATCAGATGTGTGTGATGAAACTGGAGAGCTGGGCCCACGTCTTCCG
1079 964	GGACTACAGCGTGTCTTTTCAGGTGCGATTGACGTTCACCGAGGCCAATAACCAGACTTA
1139 1024	CACCTTCTGCACCCATCCCAATCTCATCGTTTGAGCCCGTCGCGCGCG
1199	AAAACCGCGCGTCATGAGTCCCAAAAACCTGACGCCGTTCTTGACGGCGTTGTGGCTGCT
1259 1144	ATTGGGTCACAGCCGCGTGCCGCGGGTACGCGCAGAAGAATGTTGCGAATTCATAAACGT
1319	CAACCACCCGCCGGAACGCTGTTACGATTTCAAAATGTGCAATCGCTTCACCGTCGCGTA
1379	CGTATTTTCATGATTGTCTGCGTTCTGTGGTGCGTCTGGATTTGTCTCTCGACGTTTCTG

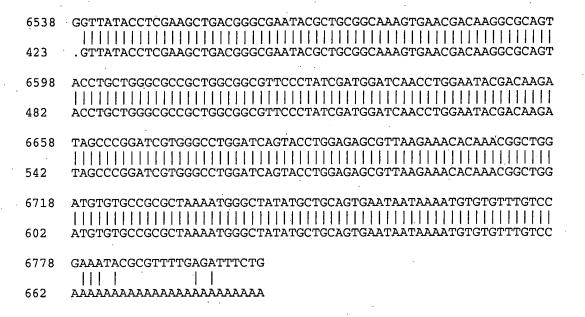
1262	
1439	ATAGCCATGTTCCATCGACGATCCTCGGGAATGCCAGAGTAGATTTTCATGAATCCACAG
1262	· · · · · · · · · · · · · · · · · · ·
1499 1262	GCTGCGGTGTCCGGACGCGAAGTCTGCTACAGTCCCGAGAAAACGGCTGAGATTCGCGG
1559 1321	GATCGTCACCACCATGACCCATTCATTGACACGCCAGGTCGTACACAACAAACTGACGAG
1619 1381	CTGCAACTACAATCCGTAAGTCTCTTCCTCGAGGGCCTTACAGCCTATGGGAAAGTAAGA
1679	CAGAGGGACAAAACATCATTAAAAAAAAAGTCTAATTTCACGTTTTGTACCCCCCCTTCC
1396	
L739 L396	CCTCCGTGTTGTAGGTTATACCTCGAAGCTGACGGGCGAATACGCTGCGGCAAAGTGAAC
L799 L442	GACAAGGCGCAGTACCTGCTGGGCGCCGCTGGCAGCGTTCCCTATCGATGGATCAACCTG
L859 L502	GAATACGACAAGATAACCCGGATCGTGGGCCTGGATCAGTACCTGGAGAGCGTTAAGAAA
1919 1562	CACAAACGGCTGGATGTGTGCCGCGCTAAAATGGGCTATATGCTGCAGTGAATAATAAA

## Comparison SEQ 128 B - FIX genomic sequence

Upper line: FIX genomic sequence

Lower line: SEQ 128 B

5998 1	ATGAGTCCCAAAAACCTGACGCCGTTCTTGACGCCGTTGTGGCTGCTATTGGGTCACAGC
6058 61	CGCGTGCCGCGGGTACGCGCAGAAGAATGTTGCGAATTCATAAACGTCAACCACCCGCCG
6118 121	GAACGCTGTTACGATTTCAAAATGTGCAATCGCTTCACCGTCGCGTACGTA
6178 181	TTGTCTGCGTTCTGTGGTGCGTCTGGATCTGTCTCTCGACGTTTCTGATAGCCATGTTCC
6238 241	ATCGACGATCCTCGGGAATGCCAGAGTAGATTTTCATGAATCCACAGGCTGCGGTGTCCG
6298 301	GACGGCGAAGTCTGCTACAGTCCCGAGAAAACGGCTGAGATTCGCGGGATCGTCACCACC
6358 361	ATGACCCATTCATTGACACGCCAGGTCGTACACAACAAACTGACGAGCTGCAACTACAAT
6418	CCGTAAGTCTCTTCCTCGAGGGCCTTACAGCCTATGGGAAAGTAAGACAGAGGGACAAAA
6478	CATCATTAAAAAAAAGTCTAATTTCACGTTTTGTACCCCCCCTTCCCCTCCGTGTTGTA
423	



#### Translation of SEQ128 B x 1.txt: HCK-3 (pUL128x1)

1	ATGAGTCCCAAAAACCTGACGCCGTTCTTGACGGCGTTGTGGCTGCTATTGGGTCACAGC
1	MSPKNLTPFLTALWLLLGHS
61	CGCGTGCCGCGGGTACGCGCAGAAGAATGTTGCGAATTCATAAACGTCAACCACCCGCCG
21	R V P R V R A E E C C E F I 🗓 V 🗓 H P P
121	GAACGCTGTTACGATTTCAAAATGTGCAATCGCTTCACCGTCGCGTACGTA
41	ERCYDFKMC 🗓 RFTVAYVFS *

# Comparison SEQ 128 A - FIX genomic sequence

Upper line: FIX-BAC

Lower line: SEQ128 A

5998 <sup>*</sup> 1	ATGAGTCCCAAAAACCTGACGCCGTTCTTGACGGCGTTGTGGCTGCTATTGGGTCACAGC
6058 61	CGCGTGCCGCGGGTACGCGCAGAAGAATGTTGCGAATTCATAAACGTCAACCACCCGCCG
6118 121	GAACGCTGTTACGATTTCAAAATGTGCAATCGCTTCACCGTCGCGTACGTA
6178	$\tt TTGTCTGCGTTCTGTGGTGCGTCTGGATTTGTCTCTCGACGTTTCTGATAGCCATGTTCC$
166	
6238	ATCGACGATCCTCGGGAATGCCAGAGTAGATTTTCATGAATCCACAGGCTGCGGTGTCCG
166	
6298 178	GACGGCGAAGTCTGCTACAGTCCCGAGAAAACGGCTGAGATTCGCGGGATCGTCACCACC
6358 238	ATGACCCATTCATTGACACGCCAGGTCGTACACAACAAACTGACGAGCTGCAACTACAAT
6418 298	CCGTAAGTCTCTTCCTCGAGGGCCTTACAGCCTATGGGAAAGTAAGACAGAGGGACAAAA
6478	CATCATTAAAAAAAAGTCTAATTTCACGTTTTGTACCCCCCCTTCCCCTCCGTGTTGTA
300	
6538 300	GGTTATACCTCGAAGCTGACGGGCGAATACGCTGCGGCAAAGTGAACGACAAGGCGCAGT
6598	ACCTGCTGGGCGCCGCTGGCAGCGTTCCCTATCGATGGATCAACCTGGAATACGACAAGA

359	ACCTGCTGGGCGCCGCTGGCAGCGTTCCCTATCGATGGATCAACCTGGAATACGACAAGA												
6658	TAACCCGGATCGTGGGCCTGGATCAGTACCTGGAGAGCGTTAAGAAACACAAACGGCTGG												
419	TAACCCGGATCGTGGGCCTGGATCAGTACCTGGAGAGCGTTAAGAAACACAAACGGCTGG												
6718	ATGTGTGCCGCGCTAAAATGGGCTATATGCTGCAGTGAATAATAAAATGTGTGTTTTGTCC												
479 ATGTGTGCCGCGCTAAAATGGGCTATATGCTGCAGTGAATAATAAAATGTG  Translation of SEQ128 A: HCK-4 (pUL128)													
Hai	instation of SEQ 128 A. HCK-4 (poe 120)												
1	ATGAGTCCCAAAAACCTGACGCCGTTCTTGACGGCGTTGTGGCTGCTATTGGGTCACAGC												
1	M S P K N L T P F L T A L W L L L G H S												
-	· ·												
61	CGCGTGCCGCGGGTACGCGCAGAAGAATGTTGCGAATTCATAAACGTCAACCACCCGCCG												
21	RVPRVRAEECCEFINVNHPP												
121	GAACGCTGTTACGATTTCAAAATGTGCAATCGCTTCACCGTCGCACTGCGGTGTCCGGAC												
41	ERCYDFKMC NRFTVALRCPD												
181	GGCGAAGTCTGCTACAGTCCCGAGAAACGGCTGAGATTCGCGGGATCGTCACCACCATG												
61	G E V C Y S P E K T A E I R G I V T T M												
241	ACCCATTCATTGACACGCCAGGTCGTACACAACAACTGACGAGCTGCAACTACAATCTG												
81	THSLTRQVVHNKLTSCNYNL												
- "													
301	$\verb TTATACCTCGAAGCTGACGGCGAATACGCTGCGGCAAAGTGAACGACAAGGCGCAGTAC $												
101	LYLEADGRIRCGKVNDKAQY												
361	CTGCTGGGCGCCGCTGGCAGCGTTCCCTATCGATGGATCAACCTGGAATACGACAAGATA												
121	L L G A A G S V P Y R W I N L E Y D K I												
	The state of the s												
421	ACCCGGATCGTGGGCCTGGATCAGTACCTGGAGAGCGTTAAGAAACACAAACGGCTGGAT												
141	TRIVGLDQYLESVKKHKRLD												

Figure 14

## Translation of SEQUL130: HCK-5 (pUL130)

1	ATG	СТА	CGG	CTT	CTG	CTT(	CGT	CAC	CAC'	TTT	CAC'	TGC	CTG	CTT	CTG'	TGC	GCG(	GTT'	TGG	GCA
.1	M	L	R	L	L.	L ·	R	Н	Н	F	Н	С	L	Ļ	L	С	A	V	W	A
61 .	ACG	CCC	TGT	CTG	GCG'	rc T	CCG'	TGGʻ	rtc.	ACG	CTA	ACG	GCG.	AAC	CAG	AAT	CCG'	rcc	CCG	CCA
21	Т	P	С	L	A	S	P	W	F	Т	L	Т	A	N·	Q	N	P	S	P	P
121	TGG	TCT.	AAA	CTG	ACG'	rat(	CCC	AAA(	CCG	CAT	GAC	GCG	GCG	ACG'	$\Gamma T T'$	rac'	rgt(	CCT	ГŤТ	CTC
41	W	S	K	L ·	<b>T</b>	Y	P	K	P	Н	D	A	Α.	<b>T</b> .	F	Y	С	P	F	L
181	TAT	CCC	TCG	ccc	CCA	CGG:	rcc	CCC	rcg	CAA'	TTC	CCG	GGG'	rTC	CAG	CGG	GTA:	rca.	ACG	GGT
61	Y	P	S	P	P	R	S	P	S	Q	F	P	G	F	Q	R	V	S	T	,G
241	CCC	GAG	TGT	CGC	AAC	GAG	ACC	CTG	rat(	CTG	CTG	TAC	AAC	CGG	GAA(	GGĊ(	CAG	ACC'	rtgo	GTG
81	P	E	С	R	N	E	Т	L	Y	L	L	Y	N	R	E	G	Q	Ť	L	V.
301	GAG	AGA.	AGC'	TCC	ACC'	rgg	GTG	AAA	AAG(	GTG	ATC	TGG'	rat(	CTG	AGC(	GGT(	CGC	TA.	CAG	ACC.
101	E	R	S	S	. <b>T</b>	W	V	K	K	V	I	M	Y	L	S	G	R	Ŋ	<b>Q</b> .	Т
361	ATC	CTC	CAA	CGG	ATG	ccc	CGA	ACG	GCT'	rcg	AAA	CCG	AGC	GAC	GGA.	AAC	GTG(	CAG	ATC	AGC
121	I	L	Q	R	М	P	R	Т	A	S	K	P	S	D	G	N .	V	Q	I	S
421	GTG	GAA	GAC	GCC2	AAG	ATT:	r <del>i</del> r(	GGA(	GC'G(	CAC	ATG	GTG	CCC	AAG	CAG	ACC	AAG	CTG	CTAC	CGT
141	V	E	D	Α	K	I.	F	G	A	Н	M	V	P	K	Q .	Т	K	L	L	R
481	TTC	GTC	GTC	AAC	GAT(	GC2	ACA	CGT.	rat(	CAG	ATG	rgr(	GTG/	ATG	AAA	CTG	GAG	AGC:	rggo	3CC
161	F	V	V	N	D.	G	Т	R	Y	Q	M	С	V	M	K	L	E	S	W	A
541	CAC	GTC'	TTC	CGG	GAC'	rac <i>i</i>	AGC	GTG'	rct:	rtt	CAG	GTG	CGA	rtga	ACG'	rtc	ACC	GAG	GCC <i>I</i>	TAA
181	Н	V	F.	R	D	Y	S	٧	S	F	Q	V	R	L	T	F	Т	E	A	N
601	AAC	CAG	ACT	rac <i>i</i>	ACC'	rrc:	rgc <i>i</i>	ACCO	CAT	CCC	YAAT(	CŤCZ	ATC	GTT.	rga					
201	N	Q	Т	Y	Т	F	C .	Т	Н	P	N	L	Į	V	*					